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OF THE CHILDREN'S HOSPITAL

WASHINGTON, D. C.

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Cases are selected from the weekly conferences held each Friday at 12:30 P.M., from the Clinicopathological conferences and from the monthly Staff meeting.

This bulletin is printed for the benefit of the present and former members of the Attending and Resident Staffs, and the clinical clerks of Georgetown and George Washington Universities.

Subscription rate is $3.00 per year. Those interested make checks payable to "Clinical Proceedings Dept.," The Children's Hospital, Washington, D.C. Please notify on change of address.

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Entered as second class matter November 21, 1946 at the post office at Washington, D.C., under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 538, Act of February 28, 1925, authorized January 17, 1947.

HYPSARHYTHMIA

Harold Stevens, Ph.D., M.D.*, George R. Dalton, M.D.†

INTRODUCTION

Hypsarhythmia is a newly identified distinctive electroencephalographic pattern characterized by a striking degree of electrographic disorganization, with marked variability in the wave form and frequency. It is further typified by random high voltages, slow waves, and spikes, the latter bearing no relationship to the slow waves. The tracing shows almost continuous diffuse dysrhythmia both during waking hours and in sleep. The frequent bursts of high voltage slow waves are often followed by generalized suppression of amplitude lasting for periods ranging from a fraction of a second, to several seconds. The spike discharges may appear in bilaterally synchronous volleys or from a focus that constantly shifts. The term hypsarhythmia, coined by Gibbs[1], means a disturbance in electroencephalographic rhythm characterized predominantly by mountainous waves (hypsi, meaning high or lofty).

The clinical significance of hypsarhythmia lies in the close correspondence between the characteristic EEG pattern and "infantile spasm", a form of convulsive disorder present in young children. These attacks are manifested by sudden violent flexion of the head and trunk, abduction or adduction of the arms, and often brief quivering of the entire body. Variants of this pattern may occur. For example, there may be sudden abduction and extension of the arms accompanied by extension of the legs, opisthotonus, and rolling of the eyes. This latter pattern has been referred to as a "cheer-leader" type of seizure[2].

The attacks may be single, but often appear in volleys. In the latter instance deep sleep often follows. The suddeness and brevity of the attacks has warranted the descriptive designation "lightning spasm" or *blitzkrampf*. Other synonyms are "massive myoclonic jerks" (Lennox & Davis)[3], "lightning major seizures" (Buchanan)[4], "generalized mass muscle jerks" (Yannet)[5]. This condition is commonly misdiagnosed, or construed as some other type of convulsive disorder. Occasionally the more classical manifestations of epilepsy are associated with hypsarhythmia; Gibbs has reported that grand mal seizures developed in 33 per cent of his 237 cases of hypsarhythmia[6]. Petit mal is readily excluded by its characteristic three per second spike wave EEG discharges. The sudden flexion spasm often accompanied by a cry might suggest the paroxysmal abdominal pain of

* Attending Staff, Children's Hospital. Professor and Head of Department of Neurology, George Washington University School of Medicine.

† Research Fellow in Allergy, Children's Hospital.

FIG. 1. Section of EEG showing diffuse dysrhythmia, "mountainous waves", and other manifestations of hypsarhythmia.

abdominal epilepsy[7], but again, the age distribution and typical electrographic pattern is diagnostic. Psychiatric syndromes have to be considered in the differential diagnosis particularly since laughter is sometimes part of the epileptic attack[2, 8, 9].

The following case typifies the syndrome of hypsarhythmia.

A five month old girl was admitted to Children's Hospital for the first time on August 13, 1956 with a history of "shaking spells". The mother described the above as beginning three weeks previously when she saw the infant draw in her lower lip, emit a cry, roll her eyes back so that only the sclerae were visible and then extend her head. The upper and lower extremities extended, and there was generalized shaking which was then followed by sleep. These brief episodes increased and occurred up to six times a day. Following admission to the hospital, even more frequent attacks were observed; these usually lasted ten to fifteen seconds each.

The patient's mother had had an urticarial reaction to penicillin injection prior to her pregnancy. In the sixth month of pregnancy with this child she was given another penicillin injection and in a few minutes became unconscious. Hospitalization was required for ten days and vigorous methods were employed to control the anaphylactoid reaction. At term, labor and delivery were normal.

In the first few months of life, the infant cried constantly and numerous formula changes were required. She appeared hungry, but had difficulty swallowing. There was frequent spitting up and vomiting.

There was no history of familial diseases. Two siblings, aged 4 and 6 years were normal.

On examination the infant appeared quite irritable. Her weight was 14½ pounds.

The head was normal in size and configuration. Bilateral blepharospasm and rotatory nystagmus were observed. Pupillary reflexes were sluggish, and there was lack of control of fixation. Bilateral optic atrophy was present. The deep tendon reflexes were hyperactive throughout. There was bilateral ankle clonus and Babinski signs.

Spinal fluid examination was negative.

An EEG showed hypsarhythmia. (Figure 1)

DISCUSSION

The apparent onset of infantile spasms several weeks after birth, while typical of this syndrome, poses a difficult diagnostic problem. If, as in many cases, the onset occurs later, i.e., several months after birth, preceded as usual by an interval of normal development, and followed by progressive intellectual deterioration, the diagnosis may be further complicated. The demonstration of the typical EEG pattern of hypsarhythmia is of substantial diagnostic and prognostic importance.

A report on gross and microscopic appearance of the brain and further neuropathological and clinical correlations in patients with this entity is in press[10].

As noted, there was abundant evidence of organic brain disease in this case, an observation made by all of the authors who have reported instances of this entity. The occurrence of bacterial or virus disease in the mother during gestation has been offered as a possible etiological factor. Anoxia

FIG. 2. Section of EEG showing another form of hypsarhythmia, with brief intervals of amplitude suppression as well as the other features.

associated with uterine bleeding during pregnancy appears to be the commonest cause according to Druckman[2]. The serious anaphylactoid reaction noted in the above case is a plausible, but not proven causative agent in this present case. Gibbs, et al., suggest encephalitis or birth trauma[6]. Illingsworth minimizes the role of birth trauma[11].

Prognosis is poor. The epileptic manifestations tended to decrease with increasing age in the children followed by Gibbs and co-workers[6]. This was associated with corresponding diminution in the hypsarhythmic pattern. However, 11 per cent died before the age of three years, and 87 per cent became mentally deficient. The child whose case is presented, at age 1½ years is unable to stand or sit, and there is un equivocal evidence of retardation.

Control of the seizures with medication is usually unsuccessful. Druckman, et al., recommend a combination of Gemonil® and Mebaral®[2]. Livingston has had good results with a ketogenic diet[12]. Gibbs, et al., report that antibiotics have helped some of their patients[6].

Associated lesions of the brain if present should be corrected. This occurred in the case of G. H., whose EEG is presented in Figure 2; in this infant a subdural hematoma was found on the right side.

SUMMARY

Attention is directed to a new epileptic disorder manifested by a combination of infantile spasms and the specific EEG pattern known as hypsarhythmia. The latter is recognized as a distinctive EEG entity, and is found exclusively in infants or young children, most of whom appear normal at birth. The dysrhythmia tends to disappear with age and correspondingly the seizures diminish. However, mental retardation is a very frequent sequel and a poor prognosis is implied when a diagnosis of hypsarhythmia is made. Other types of convulsive episodes may precede or accompany infantile spasm.

Organic brain damage of various types usually co-exists.

Drug therapy for the seizures is usually unsuccessful or only partially ameliorative. Ketogenic diet may be of help.

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SOME COMMENTS ON THE LACK OF SYNERGISM OF TETRACYCLINE-OLEANDOMYCIN MIXTURE (SIGMAMYCIN)

Sydney Ross, M.D.*, Edmund A. Zaremba, M.S.†, Jose R. Puig, M.D.‡

Rationale for the introduction of PA 775 (Sigmamycin), a combination of two parts tetracycline and one part oleandomycin, was based on the work of English, et. al.[1], who reported enhanced activity of the mixture both *in vitro* and *in vivo* over that of its individual components. These investigators reported that the synergistic action of PA 775 exceeded that of its individual components against 21 clinical isolates of staphylococci *in vitro*. In each instance, it was found that the minimal inhibitory concentration of PA 775 was less than that of either tetracycline or oleandomycin when used independently. The differences were found to be most marked when the organism was resistant to one of the two antibiotics.

In an effort to re-examine this claim of synergism for PA 775, a study embracing both an *in vitro* and *in vivo* approach was undertaken.

METHODS AND MATERIALS

The *in vitro* segment of the present investigation consisted of a determination of the minimal inhibitory concentrations of PA 775 and each of its constituents, tetracycline and oleandomycin, for 166 clinical isolates of staphylococci which had been cultured from ward patients at Children's Hospital. The serial tube dilution method for sensitivity determinations

From The Research Foundation of Children's Hospital, Washington, D. C. We are indebted to Mr. Charles Tappin for his technical assistance.

This paper has already appeared in the Antibiotics Annual (1957–1958) and is reprinted with the permission of Dr. Henry Welch.

* Attending Staff, Children's Hospital.
† Bacteriologist, Research Foundation, Children's Hospital.
‡ Resident, Children's Hospital.

was employed. Initially, all of these cultures of staphylococci were phage typed and seventeen various strains, predicated on phage pattern, were found.

The *in vivo* portion of the present study was performed by comparing the antibacterial activity of serum in the same subjects after ingestion of PA 775, tetracycline alone and oleandomycin alone in a triple cross-over study. The antibacterial action of the serum was thought to provide an index of the therapeutic value of antibiotics administered systemically. This is essentially an *in vivo* assay, *in vitro* procedures being used only for the purpose of determining the *in vivo* response.

In this triple cross-over study, fifteen young healthy men and women ranging in age from 22 to 35 years (with an average weight of 63 Kgms.) were given in random rotation a single dose of either oleandomycin (250 mgms.), tetracycline (500 mgms.) or PA 775 (750 mgms.). The experiment was conducted on the Monday of each consecutive week for three weeks. Three groups of five subjects each received the same drug on the same day and were rotated through the three antibiotic preparations, each subject thus serving as his own control. The cross-over technique was employed in order to neutralize any errors resulting from individual variation in the ability of the subjects to absorb, excrete and metabolize the drugs in question. Each subject received a dose of one of the test antibiotics one half hour before breakfast and venous blood was drawn at 0, 1, 2, 5 and 8 hour intervals. The specimens were promptly centrifuged and the sera were divided into two portions and stored at $-20°$ C. until the antistaphylococcal and antistreptococcal activity assays were performed. The latter were done according to the method described by Jones and Finland[2, 3, 4] with minor modifications. Two-fold dilutions of sera, in 0.5 ml amounts, were made in trypticase soy broth (BBL) and each specimen was assayed with two test organisms, Streptococcus # 2 (a strain of B. hemolytic streptococcus from our laboratory) and Staphylococcus 209 P (obtained from Division of Antibiotics, Food and Drug Administration). The organisms were allowed to grow overnight and then 0.5 ml of a 10^{-4} dilution of the Staphylococcus test strain and a 10^{-2} dilution of the Streptococcus test strain was added to the diluted sera. After allowing the tubes to incubate for 20 to 24 hours at 37° C. they were examined for growth; the antibiotic activity of each specimen of serum was expressed as the maximum dilution of the serum that yielded no growth.

RESULTS

I) *In Vitro Comparison of the Minimal Inhibitory Concentrations of PA 775 Tetracycline and Oleandomycin*

Table 1 summarizes data on the minimal inhibiting concentrations of oleandomycin, tetracycline, and PA 775 on 166 clinical isolates of *Staphylo-*

TABLE 1

Sensitivities of 166 Clinical Isolates of Micrococcus Pyogenes Var. Aureus to Oleandomycin, Tetracycline and PA 775. Minimum Inhibiting Concns in Mcgms/ml

	0.39	0.78	1.56	3.12	6.25	12.5	25	50	100	>100
Oleandomycin	1	38	99	27	0	0	0	0	1	0
Tetracycline	11	76	9	0	0	0	0	1	7	62
PA 775	20	77	10	19	36	3	0	0	1	0

TABLE 2

Sensitivities of 96 Tetracycline-Sensitive *Clinical Isolates of Micrococcus Pyogenes Var. Aureus to Oleandomycin, Tetracycline and PA 775. Minimum Inhibiting Concns in Mcgms/ml*

	0.39	0.78	1.56	3.12	6.25	12.5	25	50	100	>100
Oleandomycin	1	18	69	8	0	0	0	0	0	0
Tetracycline	11	76	9	0	0	0	0	0	0	0
PA 775	20	76	0	0	0	0	0	0	0	0

coccus aureus. Tables 2 and 3 summarize data on 96 of these isolates which were *tetracycline-sensitive* and 70 isolates which were *tetracycline-resistant*.

Of the 96 tetracycline-sensitive staphylococci (Table 2), the minimal inhibitory concentrations for PA 775 were identical with tetracycline in 73 strains, one tube lower in 20 strains and one tube higher than tetracycline in 3 strains. The close parallel in sensitivities suggests that the inhibitory effect of PA 775 in this group of organisms was primarily a function of its major constituent tetracycline. In the 20 strains where PA 775 showed a greater inhibitory effect than tetracycline, the disparity was in no instance greater than a one tube difference; this can hardly be regarded as significant since it has been pointed out that even under rigid test conditions, duplication of results with the serial tube dilution method may be obtained within a two-fold error[5].

Of the 70 tetracycline-resistant staphylococci (Table 3), the minimal

TABLE 3

Sensitivities of 70 Tetracycline-Resistant *Clinical Isolates of Micrococcus Pyogenes Var. Aureus to Oleandomycin, Tetracycline and PA 775. Minimum Inhibiting Concns in Mcgms/ml*

	0.39	0.78	1.56	3.12	6.25	12.5	25	50	100	>100
Oleandomycin	0	20	30	19	0	0	0	0	1	0
Tetracycline	0	0	0	0	0	0	0	1	7	62
PA 775	0	1	10	19	36	3	0	0	1	0

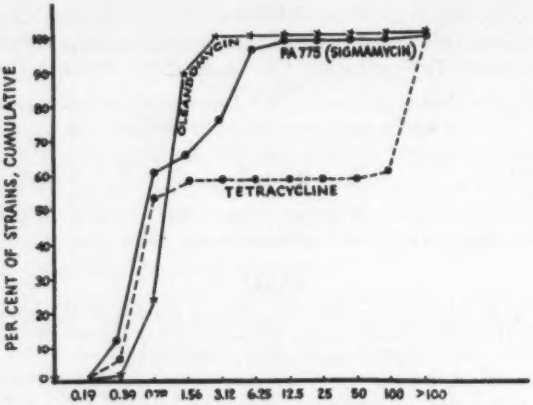
PA 775 (SIGMAMYCIN)
OLEANDOMYCIN
TETRACYCLINE
PER CENT OF STRAINS, CUMULATIVE
0.19 0.39 0.78 1.56 3.12 6.25 12.5 25 50 100 >100
MINIMUM INHIBITING CONCENTRATION (MCGMS/ML)

FIG. 1. Sensitivity of 166 strains of micrococcus pyrogenes var. aureus to {PA 775 (sigmamycin) •——•; tetracycline •- - -•; oleandomycin •——•}

inhibitory concentrations for PA 775 were identical to oleandomycin in 2 strains, one tube higher in 38 strains and two tubes higher than oleandomycin in 30 strains. The inhibitory effect of PA 775 in this group of organisms was thought to be due to the oleandomycin content of the combination. It should be noted that PA 775 did not demonstrate a greater inhibitory effect than oleandomycin against a single one of these 70 tetracycline-resistant staphylococci. This is especially significant in that it fails to bear out the findings of English, et al.,[1] who reported that PA 775 showed *in vitro* synergistic activity most markedly in instances where the organism was resistant to one of the two constituent antibiotics.

From these data, the conclusion seems warranted that the inhibitory effect of PA 775 is primarily due either to the tetracycline or oleandomycin portion of the mixture and further that the combination per se fails to exert any synergistic activity in the *in vitro* studies described above. Fig. 1 delineates this finding rather graphically.

II) *Comparison of the Antibacterial Activity of Serum after Ingestion of PA 775, Tetracycline and Oleandomycin*

Fig. 2 shows the *mean* antistaphylococcal activity of the 15 subjects with each of the three antibiotic preparations. The values are represented as the reciprocals of the dilutions. As will be observed, the antistaphylococcal activity of the sera after 750 mgms. of PA 775 rose to peak levels after 2 hours, remained at this level during the next 3 hours and then tapered off. The antistaphylococcal activity curve with 500 mgms. of tetracycline

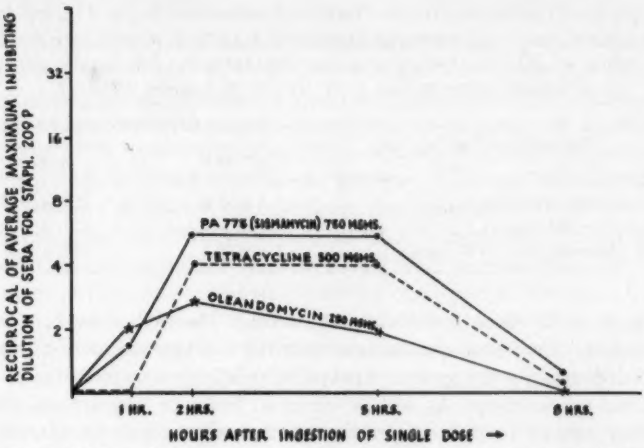

FIG. 2. Inhibition of staph. 209 P by sera after ingestion of tetracycline, oleandomycin or oleandomycin-tetracycline mixture (PA 775)

paralleled closely the PA 775 curve after the first hour. The antistaphylococcal activity after ingestion of 250 mgms. of oleandomycin showed a low peak activity after 2 hours followed by a gradual tapering off over the course of the next six hours.

Fig. 3 depicts the *mean* antistreptococcal activity of the 15 subjects

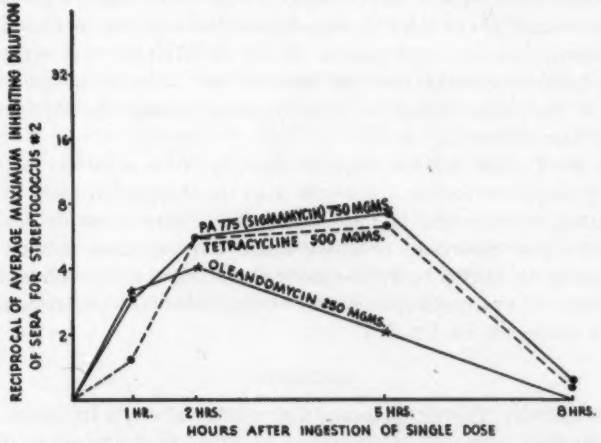

FIG. 3. Inhibition of streptococcus #2 by sera after ingestion of tetracycline, oleandomycin or oleandomycin-tetracycline mixture (PA 775)

TABLE 4

Average Antistreptococcal and Antistaphylococcal Activity of Serum after a Single Oral Dose of PA 775, Tetracycline and Oleandomycin. The Results are Presented as the Average of the Number of Twofold Dilutions

Antibiotic and Dose	Average Maximum Inhibiting Dilutions of Serum ± *SD*	
	Staph. 209 P	Strep. #2
Oleandomycin (250 mgm)	1.5 ± 0.2	2.3 ± 0.2
Tetracycline (500 mgm)	2.5 ± 0.3	3.0 ± 0.3
PA 775 (Sigmamycin) (750 mgm)	2.9 ± 0.2	3.0 ± 0.3

with each of the three antibiotic preparations. The higher levels of inhibitory activity than those encountered with the staphylococcus test organism were a reflection of the greater susceptibility of the streptococcus to these antibiotic preparations. As will be observed however, the general pattern was very similar to that observed with the antistaphylococcal activities (Fig. 2) except for the even closer correspondence between tetracycline and PA 775 antistreptococcal activities.

The average value for the peak concentrations of antistaphylococcal and antistreptococcal activity against the two test strains are presented in Table 4. These values are expressed as the maximum number of two-fold dilutions of sera that inhibited these test organisms.

As may be seen, the average peak concentration of antistaphylococcal activity was highest with PA 775, somewhat less with tetracycline and lowest with oleandomycin. Statistically however, the slightly greater antistaphylococcal effect of PA 775 seemed to reflect only the increased dosage level employed in the combination. As for antistreptococcal activity, the average peak concentrations were identical for tetracycline and PA 775 in spite of the higher dosage of the latter and, as might be expected, were lower for oleandomycin.

These data would indicate that the activity of the combination PA 775 is, to a first approximation, consistent with the separate activity of its two constituents, tetracycline and oleandomycin. There is no definitive evidence for either synergism or antagonism. The principal activity of PA 775 appeared to be due to the presence of the tetracycline. These findings would support the previously described *in vitro* data controverting the claims of synergism for PA 775.

DISCUSSION

It is manifestly difficult to assess the validity of any clinical study purporting to show evidence of synergism resulting from the use of PA 775. There have been several studies reported[6, 7, 8, 9] which have reached this conclusion but critical analysis of the results fails to ascribe to each com-

ponent drug of the combination its individual contribution to the salutary clinical results. The lack of a control study has been the common denominator of these clinical reports. If, for example, one were to use PA 775 in 50 cases of pneumococcal pneumonia and report good results with this preparation, may one ascribe this favorable outcome to the combination? Without suitable controls, such a report would be virtually worthless as an index of the efficacy of combination antibiotic therapy. If, on the other hand, one were to manage 50 cases of pneumococcal pneumonia with PA 775, another 50 cases with tetracycline and a third group of 50 cases with oleandomycin, and after careful statistical analysis, one could demonstrate significant differences in therapeutic response favoring combination therapy, then acceptance of such a claim for synergism would be substantially more palatable. Up to the present writing however, no such controlled clinical studies have been forthcoming, and hence the Scotch verdict of "not proven" must be rendered.

If the clinical evidence for synergism by PA 775 has been unimpressive, the laboratory evidence has even been less so. Levitt and Hubble[10] recently described their study of 30 strains of staphylococci in which they showed that against no strain was PA 775 more effective, *in vitro*, than either of its component parts. They concluded that synergism was not demonstrated *in vitro* between tetracycline and oleandomycin in a combination ratio of 2:1. Arriving at much the same conclusion from his own *in vitro* studies, Garrod[11] states that "not in a single instance was the minimal inhibitory concentration of the combination (PA 775) lower than that of one of its constituents acting alone". He concludes that "these experiments have failed to demonstrate the synergistic action claimed for the tetracycline-oleandomycin combination".

Our own *in vitro* results would be in complete agreement with these two reports. Against 166 strains of staphylococci, our data failed to show a single instance of *in vitro* synergistic activity with PA 775. The antibacterial effect appeared to be a function of either the tetracycline or the oleandomycin content of the mixture.

Similarly, our *in vivo* data on the antistreptococcal and antistaphylococcal activity of sera obtained from 15 healthy adults in a controlled triple cross-over experiment after ingestion of oleandomycin, tetracycline, and PA 775 in random rotation failed to show any clear cut statistical evidence of synergism.

SUMMARY

1. In order to re-examine the claim of synergism for PA 775 (Sigmamycin), a study embracing both an *in vitro* and *in vivo* approach was undertaken.

2. The *in vitro* segment of the present investigation consisted of a de-

termination of the minimal inhibitory concentrations of PA 775 and each of its components, tetracycline and oleandomycin, for 166 clinical isolates of staphylococci which had been cultured from ward patients at Children's Hospital. PA 775 was found to exert no synergistic activity *in vitro* and it appeared that the inhibitory effect of PA 775 was primarily due to either the tetracycline or oleandomycin portion of the mixture.

3. The *in vivo* part of the present study was performed by comparing the antistaphylococcal and antistreptococcal activities of serum in 15 young healthy adults after ingestion of PA 775, tetracycline alone, and oleandomycin alone in a triple cross-over study with each subject serving as his own control. The results indicated that the antibacterial activity of sera after ingestion of PA 775 was consistent with the separate activity of its two components, tetracycline and oleandomycin. There was no definitive evidence of synergism and the principal activity of PA 775 appeared to be due to the presence of its major component tetracycline.

4. Both the *in vitro* and *in vivo* data appeared to controvert the claims of synergism for PA 775.

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THE POISON CONTROL CENTER

Allan B. Coleman, M.D.*, James Goddard, M.D.†

In the United States today, accidents are the leading cause of death in all ages from one to thirty five years. In addition, there are approximately nine million persons injured each year, some three hundred of whom are permanently disabled. Accidental poisoning accounts for about 2 per cent of fatalities and about 5 per cent of the morbidity. In 1954 there were 435 deaths from poisoning by solid or liquid substances in the age group of one through 19 years in the continental United States. The bulk of these, 80 per cent, or 341 cases occurred in children under five years of age. Aspirin and petroleum products are two of the chief offenders, probably accounting for 15 and 10 per cent respectively of the total number of fatalities. There are no satisfactory morbidity data to approximate the number of non-fatal cases of poisoning, but estimates vary from 100 to 200 non-fatal cases to each fatality.

The District of Columbia Poison Control Center is in its fourth year, having been organized as the second such program in the United States. It was stimulated by a similar program started in Chicago by Dr. Edward Press. The local center has attempted to fulfill the purposes of a municipal or regional poison control center which include the systematic collection of statistical data on accidental poisoning, and furnishing technical information to physicians and other medical facilities. Such information includes the proper methods of treating poisoning from various noxious substances, but more important, the content of common household products with reference to toxic substances.

The Center has been located, since its inception, in the Out Patient Department of Children's Hospital. The program has been a modest one, operating with borrowed facilities and few funds. It has been possible,

* Associate Staff, Children's Hospital; Associate in Pediatrics, George Washington University.

† Lecturer, George Washington University School of Medicine. Chief of Accident Prevention Program, Division of Special Health Services, Bureau of State Services, Public Health Service, United States Department of Health, Education and Welfare.

however, to establish a community service by gradually accumulating a reference library (recently considerably expanded), and rapidly furnishing information requested by telephone. The local center is unique in having additional valuable sources from which to draw information on poisons. The newly established National Clearinghouse for Poison Control Centers is physically located in the District of Columbia. The United States Department of Agriculture has available various facilities to provide information on poisonous plants, animals, and insects. The National Zoological Park has always been available for counseling on snake and other venomous reptile poisoning and has made antivenin promptly available.

The National Clearinghouse for Poison Control Centers has recently been established as an agency of the Public Health Service. Since the establishment of the first center in Chicago there has been a phenomenal growth in the poison control center movement throughout the country. At the present time there are 110 local poison control centers located in 36 states in the United States. It was recognized as early as 1955 that there would be a need for the coordination of information among these local centers to provide unnecessary duplication of effort. Accordingly, the American Academy of Pediatrics, the American Public Health Association, and the American Public Health Association Committee on Chemical Poisons combined forces and conducted an intensive investigation into the needs for a national clearinghouse for poison control centers. This investigation culminated in a request to the Secretary of Health, Education, and Welfare to establish such a center.

The National Clearinghouse for Poison Control Centers was organized with several objectives in mind. The first objective is to provide an easy means of interchanging information among existing poison control centers with particular reference to new methods of treatment and the constituents of new "trade name" products encountered in a given community. A second objective is to stimulate new methods of prevention and treatment of poisoning. Emphasis should be placed on the importance of the development of new methods of *prevention*. The objective of the local center is primarily to assist the physician in the diagnosis and treatment of an individual case of poisoning and is therefore best termed secondary prevention. The National Clearinghouse hopes to develop means of prevention of poisoning in the first place. The third objective is to assist local communities and states in establishing poison control centers. Some guidance needs to be given to the great number of centers mushrooming all over the United States. It may be more economical to establish one major center in a given state and several small centers in hospitals in the larger cities rather than a center in every community within the state. A fourth objective is to study both state and national trends in the occurrence of accidental poisoning,

and the fifth objective is to provide a single location where manufacturers could provide information which could then be turned over to local centers.

The magnitude of cataloguing common household products is overwhelming. There are over 250,000 household "trade name" products on the market today and these are being added to by 5,000 to 10,000 per year. The legal requirements are such that manufacturers do not have to include on many of the products' labels the proportions of the ingredients contained in the product, or even the ingredients themselves. The National Clearinghouse for Poison Control Centers has developed a uniform recording system of such products, and it is the hope that the local poison control centers, utilizing such a recording system will also provide comparable data from the various areas of the United States. Full and accurate recording is recognized as essential in trying to carry out any control studies on a community basis.

The National Clearinghouse is also preparing monthly bulletins on new products, changes in treatment, and any general information which will be of use to the local poison control center. Statistical services are also being made available to analyze case loads and types of poisoning as recorded by the various local centers. The National Clearinghouse is developing and will soon make available to local centers a card file which will provide some 500 to 700 common ingredients or substances which account for about 95 per cent of all poison cases.

The need for additional research into factors entering into various aspects of accidental poisoning is great. The National Clearinghouse is interested in supporting research projects which lead to a better understanding of how to prevent poisoning in a given community. A project currently underway by a local health department in California is attempting to investigate every case of poisoning to try to determine some of the antecedents. Its control group is drawn from cohorts in the neighborhood and an intensive study is being made of the various sociological and psychological factors entering into each case of accidental poisoning. It is hoped that some answer may be forthcoming to the question of how mothers can be convinced to store potentially poisonous products properly. It is felt that in investigating factors entering into the control of accidental poisoning in childhood, a very specific and tangible portion of the whole problem of accident prevention may be dealt with in a relatively short period of time. If the physicians, health departments and hospitals in the United States meet their responsibilities and work together, it is not inconceivable that in a three year period we will see approximately one-third reduction in the number of fatalities from accidental poisoning and an equally significant reduction in the number of non-fatal cases.

EDITORIAL

The Poisoning Control Concept

Robert H. Parrott, M.D.*

In our day of mass public appeals for funds for medical causes, a pronouncement that there are as many as 2083 deaths in one year due to accidental poisoning, could be considered of low dramatic value. Isn't a disease such as cancer, or cystic fibrosis, or heart disease worse? True, accidental poisoning figures can be dramatized by computing that there are 89,761 man-years lost due to poisoning deaths in one year. The problem may also be pointed up by saying that there are as many as 100 times as many poisonings as there are deaths due to poisoning. Nonetheless, the statistics, even as they improve, do not tell the whole tale. The important and sad fact is that each one of these deaths and illnesses is capable of being prevented! None of them need to have occurred!

It is possible to over simplify the problem of accidental poisoning in children to three elements:

The Child: A child in the age group most susceptible to poisoning will, by his very nature, try anything once. He is learning, exploring, trying, reaching, climbing, tasting; and if a toxic substance is within the day's wanderings he will try it too. Even older children are inquisitive and will by nature "test the rules" or taste something that looks good or smells good.

The Poison: If the child is to be poisoned, a potential poisonous substance must be available to him. Conversely, poisoning will not occur if such material is safely locked or kept out of his reach. Toxic materials are not only made available to children but are often dressed up in taste, color, and container to render them more attractive, for example, the candied antipyretics or the furniture polish kept in a soft drink bottle.

The Environment: The child who has ingested a poisonous material cannot be considered apart from his environment. It is failure of environment, failure of parental control, which permits the child to gain access to the poison. In most instances this results from carelessness or ignorance of facts about the behavior of children or the potential toxicity of certain materials.

The ultimate object of any poisoning control program is prevention, to separate the child from potential poisons through his parents; but treatment, pooling of treatment information, research, and educational promotion are vital parts of the concept. Any well functioning program must

Reprinted with permission from HOSPITALS, Journal of the American Hospital Association, **32**: 37, January 16, 1958.

* Physician-in-Chief, Children's Hospital.

make its services available to all physicians, health personnel, and medical facilities in an area. This also means, however, that such individuals and facilities must *share* the concept and cooperate with the program. It is suggested that the poisoning control concept can prevail and be truly effective only if each individual physician, health officer, hospital administrator, hospital pharmacist, whether or not he is directly connected with a formal program, will consider that he is responsible for his own poisoning control program. The physician might inspect the medicine cabinets of his patients as he makes home calls; the health officer might assure that his department is offering proper case follow-up, public information and laboratory services; the administrator that his out patient service is properly equipped to manage accidental poisoning cases; the pharmacist that he has a reasonable file of poisoning information, that he is labelling his prescriptions to "keep out of the reach of children".

In brief, accidental poisoning is preventable. Basically the problem is to keep the child away from potential poisons. All have a stake in the problem and each of us can help by practicing the poisoning control concept within his own scope of activities.

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